

EXHIBIT B



Advancing Therapeutics.
Improving Lives.

Linnea Tanner
Director, Regulatory Affairs

13 December 2006

Norman L. Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Food and Drug Administration
Center for Drug Evaluation & Research
Central Document Room
5901-B Ammendale Rd.
Beltsville, MD 20705-1266

Subject: **NDA 22-081 (022081-0000)**
LETAIRIS™ (ambrisentan) Tablets

NEW DRUG APPLICATION
Original Submission

Dear Dr. Stockbridge:

Pursuant to the Paragraph 505(b)(1) of the Federal, Food, Drug and Cosmetic Act (the ACT) and 21 CFR 314.50, Gilead Sciences, Inc. (Gilead) hereby submits a New Drug Application (NDA) for LETAIRIS (ambrisentan) Tablets, 5 and 10 mg. Ambrisentan is a non-sulfonamide, propanoic acid-class, endothelin receptor antagonist (ERA) that is selective for the endothelin type A (ETA) receptor. LETAIRIS is indicated for the treatment of pulmonary arterial hypertension (WHO Group 1) to improve exercise capacity, delay clinical worsening and improve symptoms.

Myogen, Inc. was acquired by Gilead Sciences, Inc. and became a wholly owned subsidiary known as Gilead Colorado, Inc., effective November 17, 2006. Thus, the NDA applicant is Gilead Sciences, Inc., which assumes all the responsibilities and obligations of the NDA. However, the name Myogen, Inc. is used throughout the NDA for historical reasons and because of the timing of acquisition.

Request for Priority Review

Ambrisentan was granted Fast Track designation for the treatment of pulmonary arterial hypertension (PAH) on February 15, 2006; therefore, we request that this application be given priority review. PAH is a rare, serious and life-threatening disease for which there is no cure. Although there are other therapies currently approved for this disease, there still is an unmet medical need for the treatment of PAH. LETAIRIS is an alternative, therapeutic option for these patients that has the potential to provide significant benefit over currently authorized therapies for the following reasons:

Confidentiality Statement

The confidential information contained in this document is the property of Gilead Sciences, Inc. Your acceptance of this document constitutes agreement that you will not disclose the information contained herein to others without written authorization from Gilead Sciences, Inc.

- Improved effects on exercise capacity, an efficacy measure that has been shown to correlate with and be prognostic of long-term survival
- Significant delay of the clinical worsening of PAH, an efficacy measure of disease progression in this ultimately fatal disease
- Improved effects on symptoms associated with PAH (WHO functional class, Borg dyspnea index, and SF-36[®] physical function scale)
- Low incidence of liver function test (LFT) abnormalities, a serious toxicity that can lead to discontinuation of treatment with other ERA therapies
- Potential to provide benefit to PAH patients who have previously discontinued ERA therapy due to LFT abnormalities
- No clinically significant cytochrome P450 (CYP) enzyme-related interactions with several drugs that are currently contraindicated, less effective, or associated with significant safety issues when co-administered with other PAH therapies

Orphan Drug Designation

Ambrisentan was granted orphan drug designation (Designation Request #04-1836) for the treatment of PAH and, therefore, qualifies for seven (7) years of exclusive marketing rights pursuant to Section 527 of the ACT (21 U.S.C. 360 cc). A letter dated December 07, 2006 was submitted to the Office of Orphan Drug Products Development to transfer the orphan designation from Myogen, Inc. to Gilead Sciences, Inc.

Application Fee

Under Section 736(a)(1)(E) of the ACT, this NDA is not subject to an application fee because LETAIRIS (ambrisentan) Tablets, 5 and 10 mg, is indicated for the treatment of a rare disease or condition designated under Section 526 of the ACT (orphan drug designation).

Pediatric Data

Since ambrisentan was granted orphan designation for PAH under Section 526 of the ACT (21 U.S.C. 360bb), no pediatric data is submitted in the original NDA 22-081. Pediatric data is not required for applications to market the product for the orphan-designated indications and a waiver is not needed [21 CFR 314.55(d) for NDAs and 601.27(d) for BLAs]. As agreed during the Pre-NDA meeting on May 19, 2006, Gilead will submit a pediatric study request and a proposal for a pediatric study following the NDA submission so that the Division can issue a written request to initiate pediatric studies that will be used to support pediatric exclusivity.

Proposed Proprietary Name

The proposed proprietary name of LETAIRIS was submitted for review on November 4, 2005 in Serial No. 094 of IND 64,915.

Application Format

The archive copy of NDA 22-081 (eCTD 022081-0000) is provided in its entirety as an electronic submission using the electronic Common Technical Document (eCTD) format in accordance with the guidance *M2: eCTD: Electronic Common Technical Document Specification* and as agreed in the Pre-NDA meeting on May 19, 2006. Gilead has notified the FDA Denver District office about the NDA submission in the eCTD format. A copy of the field copy certification is provided in Section m1.3.2.

Please refer to an attachment (Summary of FDA Interactions and Commitments for Ambrisentan Development Plan) to this cover letter for any other agreements of the format and content of the NDA, including the electronic datasets.

Required Regulatory Forms applicable to this submission have been included in the electronic submission and are signed electronically. Pursuant to 21 CFR 11.100, Gilead certifies that all electronic signatures executed by our employees, agents, or representatives, located anywhere in the world, are the legally binding equivalent of traditional handwritten signatures.

This submission is provided on a DVD-ROM and is approximately 4.2 GB. Gilead certifies that the submission is virus free as defined by the 11 December 2006 version of the McAfee® VirusScan® Enterprise-program, Version 8.0.0, Scan Engine 5100, with 4916 virus definitions.

Annotated ECG Waveform Data

In accordance with the instructions available on the CDER Electronic Regulatory Submissions and Review website, and confirmation with the Office of Business Process Support (OBPS), Gilead has submitted annotated ECG waveform data in XML format to the E-Scribe ECG Warehouse. These files are representative of data collected in a Phase 1 QTc study (AMB-104), and the two pivotal Phase 3 studies (AMB-320 and AMB-321). These data files are now available for your review through E-Scribe ECG Warehouse.

Contact Information

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Please do not hesitate to contact me with any questions.

Sincerely,

{See appended electronic signature page}

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Attachment: Summary of FDA Interactions and Commitments for Ambrisentan Development Plan



GILEAD

Document Approval Certificate

THE PRECEDING DOCUMENT HAS BEEN ELECTRONICALLY SIGNED BY:

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